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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/171,625 | 07/02/1999 | HUBERT KOSTER | 24743-2302US | 8272 |

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EXAMINER

PONNALURI, PADMASHRI

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1627

DATE MAILED: 05/14/2002

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/171,625

Applicant(s)
Koster et al

Examiner
Padmeshri Ponnaluri

Art Unit
1627



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Feb 22, 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4 and 11-16 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4 and 11-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

1. The election and amendment B, filed on 2/22/02 has been fully considered and entered into the application.
2. Claims 26-36 have been canceled by the amendment B, filed on 2/22/02; claims 1-3, 5-10, 17-25 have been canceled by the amendment filed on 8/31/01.
3. Claims 4 and 11-16 are currently pending and are being examined in this application.
4. Applicant's election without traverse of group I, claims 4, 11-16; and election of trityl ether as linkage, and phosphate group as reactive moiety, in Paper No. 21, filed on 2/22/02, is acknowledged.
5. This application does not contain an abstract of the disclosure as required by 37 CAR 1.72(b). An abstract on a separate sheet is required.
6. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.
7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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9. Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The linkage cleavable under 'photolytic conditions' claimed in Claim 15 has no clear support in the specification and the claims as originally filed. The specification discloses the cleavage of linkage between the supports and the monomers by the use of reagents which are acid, base or neutral. The subject matter claimed in claim 15 broadens the scope of the invention as originally disclosed in the specification.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

10. Claims 4, 11-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of specific linkers (npeoc, npc and nps) with specific reactions (deprotection reactions), does not reasonably provide enablement for any type of protecting groups and deprotection reagents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims briefly recite a process for generating a combinatorial library, by preparing a plurality of immobilized molecules (nucleoside or nucleotide), where in each

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molecule contains 3 to 10 reactive moieties, each reactive moiety is blocked by a blocking group, and at least three blocking groups on a molecule are independently removable under at least three different conditions; and removing the blocking group and derivitizing the resulting moiety in a preprogrammed, regioselective manner to generate a combinatorial library.

The specification disclosure is based on the use of specific protecting groups and specific reactions and conditions to remove the protecting groups, such that the blocking groups (protecting groups) are activated in regioselective manner. The specification pages 7- 10 disclose the selective orthogonal deprotection . The specification discloses specific protecting groups (reactive in acidic or neutral or basic conditions). The specification discloses that 'selective and orthogonal deprotection are possible if at the linkagesof oligomers, deprotections are selectively done...'. The specification disclosure is based on the use of specific protecting groups at selective positions on the molecules, such that they are regioselectively removed using deprotection reagents.

The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands* (U. S. P. Q. 2d 1400: CAFC 1988) which include: the quantity of experimentation necessary; . the amount of direction or guidance presented; the presence or absence of working examples; . the nature of the invention; the state of the prior art; the predictability of the art; and the breadth of the claims.

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A number of factors would prevent one of ordinary skill in the art from practicing (making and using) the invention without undue experimentation, which are summarized as follows:

a. The specification fails to give adequate direction and guidance as to the means of making combinatorial libraries using any type of protecting groups to protect any reactive functional groups using deprotection reagents. The specification discloses that the deprotection conditions of one specific protecting group is selected such a way so that the deprotection would not not effect the other protecting groups. The specification discloses that deprotection of npeoc/npe would not effect the trityl ether bond of npe bond. The specification discloses that the deprotection conditions has to be determined so that the conditions would not effect other protecting groups. For example, the specification discloses that 'the stability of R4 during deprotection at 1, 3 and 4 is not necessary, and if R4 is being removed during deprotection at position 4 using reagent IV,... the substitution at position 2 has to be carried out before, and R4 must be stable with reagent II, to guarantee a sequence specific derivitization at position 2. Thus, the use of protecting groups and deprotection reagents are specific, and the sequence of deprotection reactions are specific or predetermined based on the stability of the protecting groups.

b. The working examples are directed to the use of specific protecting groups and deprotection reagents or conditions.

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c. The breadth of the claims are open-ended regarding the use of protecting groups and deprotection reaction conditions, and the order of the deprotection reactions.

d. The art is inherently unpredictable because the use of protecting groups in a specific position may be unstable during the deprotection conditions, and result in unwanted reactions to occur.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

11. The following is a statement of reasons for the indication of allowable subject matter: the claimed method for generating a combinatorial library is neither taught nor suggested by the prior art. The claims are allowable if they overcome the 112, first paragraph rejections..

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR

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1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on *Increased Flex Schedule* and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, Ph.D., can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Patent Examiner
Technology Center 1600
Art Unit 1627
10 May 2002


PADMASHRI PONNALURI
PRIMARY EXAMINER